

Surgical ablation as treatment for the elimination of atrial fibrillation: A meta-analysis

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Objective: The maze procedure is recognized as the most effective surgical treatment of atrial fibrillation. In the last few years, new surgical ablation techniques were developed involving the left atrium only and modifications of the maze procedure in ablating both atria. For this study, we evaluated the evidence regarding the effectiveness of the surgical ablation procedures (biatrial and left atrial) in reducing postoperative atrial fibrillation and subsequent survival.

Methods: MEDLINE was searched for English-language studies using the terms “maze,” “atrial fibrillation,” and “surgical treatment” for 1995 through August 2005. Primary outcomes of interest were postoperative survival and postoperative freedom from atrial fibrillation. Survival data were collected at 1-, 2-, and 3-year intervals. Freedom from atrial fibrillation was collected at 3 months and at 1-, 2-, and 3-year intervals.

Results: Sixty-nine studies were included in this analysis. Five thousand eight hundred eighty-five total patients were involved. Patients undergoing surgical ablation (range, 90.4-85.4) demonstrated significantly greater rates of freedom from atrial fibrillation compared with those seen in control patients (range, 47.2-60.9). Survival rates among patients with biatrial surgical procedures (range, 94.9-92.8) were similar to those who had left atrial procedures only (range, 93.9-89.4). However, patients undergoing biatrial ablation (range, 92.0-87.1 vs 86.1-73.4) demonstrated superior freedom from atrial fibrillation at all time points.

Conclusion: Biatrial ablation surgical procedures were more effective in controlling atrial fibrillation than procedures confined to the left atrium. To encourage the use of future meta-analysis within the surgical literature, we suggest the more frequent reporting of either through Kaplan-Meier survival analyses and the reporting of rates for specific time intervals.

The maze procedure is recognized as the most effective surgical treatment of atrial fibrillation (AF). Introduced in 1987 by J. L. Cox as a stand-alone procedure, the maze procedure has undergone 4 iterations, with each successfully replacing the previous one.

To our knowledge, there have been no systematic reviews or meta-analyses to estimate and compare the efficacy of the maze procedure and any other biatrial surgical procedure with that of procedures limited to the left atrium in the elimination of AF. The goal of this study is to assess the evidence regarding the effectiveness of the different surgical ablation techniques in eliminating postoperative recurrent AF. In addition, we report postoperative survival rates for 1, 2, and 3 years.

Methods

Search Strategy

We searched MEDLINE for studies in English using the terms “maze,” “atrial fibrillation,” and “surgical treatment” for the period of 1995 through March 2005. We eliminated any case

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Abbreviations and Acronyms

AF = atrial fibrillation

reports or articles focusing on electronic advances in the surgical treatment of AF. Four studies were eliminated because they represented the same patient group. Studies were then reviewed a final time by each author to ensure the search criteria were met and desired clinical data were included.¹⁻⁶⁹

Statistical Methods

Each author then reviewed each report to dichotomize every study into temporal categories of “retrospective” or “prospective” and to assign study sample sizes to one of 3 size categories on the basis of the sample of surgical patients in each study: small (<50), medium (51-100), or large (>100). The individual author results were then compared, and differences in interpretation were resolved. Included studies reflected surgeon preference for the use of different procedures: the use of some studies using the standard maze procedure lesion set and others using different protocols for biatrial and left atrial lesion sets only. Thus we defined included surgical ablation procedures as either biatrial or left atrial procedures only.

The primary outcomes of interest were postoperative survival and postoperative freedom from AF. Survival data were collected at 1-, 2-, and 3-year intervals. Freedom from AF was collected at 3 months and at 1-, 2-, and 3-year intervals. In the event that a study involved multiple control groups, control group survival and freedom from AF estimates were combined into one control group by using weighted averages, with the respective control group sample sizes serving as the weights.

Effect sizes for all end points were calculated by using the Cohen *d* statistic.⁷⁰ Variance estimates for all end points were calculated by using the method of Hunter and Schmidt.⁷¹ Weighted postoperative survival and freedom from AF estimates were analyzed, with the respective study surgical group or control group sample sizes used as the weights. The Student *t* test was used to test for statistical significance. All statistical analyses were conducted with SAS (version 8.12; SAS, Cary, NC) software.

Results**Studies**

Sixty-nine studies were included in this analysis. Biatrial surgical ablation procedures accounted for 67% of all studies, and 75% were retrospective in nature. Small studies (<50 subjects) comprised almost one half of all studies (42%). Only 14 (19%) studies involved control groups. Average patient follow-up was 22.9 months. Primary indication for surgical intervention was prolonged AF, usually defined as “chronic,” generally presented in tabular format in the Results section or defined earlier as “chronic” or “persistent” AF lasting more than 6 or 12 months. Electrocardiography, Holter monitoring, echocardiography, or combinations of these were primarily used to define postoperative freedom from AF. Several reports relied on pa-

TABLE 1. Average sample size

Parameter	No. of studies	Mean no. of patients	Standard deviation	Range
Total no. of subjects	69	85.3	62.1	10-276
Surgical subjects only	69	74.9	59.8	5-276
Control subjects only	14	51.3	57.2	10-227
Biatrial sample size	47	73.3	61.3	5-276
Left atrial sample size	24	67.3	58.2	13-234

tient self-report during follow-up, but electrocardiographic confirmation was then obtained. Freedom from AF end points was primarily defined as a return to sinus rhythm.

Samples Size

Sample sizes for selected studies averaged 85.3 (74.9 for subjects undergoing surgical ablation and 51.3 for control subjects, Table 1). Studies with the biatrial ablation procedure averaged 73.3 subjects, and studies with left atrial procedures averaged 67.3 subjects. Sample sizes for which a control group was involved generally included more control subjects compared with surgical patients (average, 51.3 [range, 10-227] vs 37.1 [range, 5-103]).

When stratified by lesion, studies involved more patients undergoing biatrial ablation (88.0 ± 60.1) compared with patients undergoing left atrial ablation (79.9 ± 67.1 , Table 2). When stratified by temporal score, prospective studies enrolled fewer total subjects (57.8 ± 40.4) and almost one half as many surgical patients (45.0 ± 32.7) compared with retrospective studies (94.3 ± 65.6 and 84.7 ± 63.5 , respectively; Table 2).

Patient Survival and Freedom from AF, All Patients

Patients undergoing surgical ablation demonstrated similar survival rates compared with those of control patients (Table 3). At 1, 2, and 3 years, control subjects demonstrated a 3% improvement in survival. However, at 3 months and 1, 2, and 3 years, patients undergoing surgical ablation (range, 90.4%-85.4%) demonstrated significantly greater rates of freedom from AF compared with those seen in control subjects (range, 47.2%-60.9%). With the exception of the 3-year end point, surgical patients nearly doubled the freedom from AF rate compared with that seen in control subjects.

Patient Survival and Freedom From AF by Lesion

When stratified by lesion (biatrial lesions vs left atrial lesions only), survival rates among biatrial surgical patients (range, 94.9%-92.8%) were similar to those among left atrial surgical patients (range, 93.9%-89.4%; Table 4). Biatrial surgical patients (range, 92.0%-87.1%) demonstrated superior freedom from AF at all time points compared with left atrial surgical patients (range, 86.1%-73.4%).

TABLE 2. Average sample size by lesion and temporal score

	Biatrial			Left atrial			<i>P</i> value
	No. of studies	Mean \pm SD	Range	No. of studies	Mean \pm SD	Range	
Total subjects	46	88.0 \pm 60.1	10-276	23	79.9 \pm 67.1	13-234	.312
Surgical subjects	46	79.0 \pm 59.6	10-276	23	66.6 \pm 60.5	5-234	.210
Control subjects	10	41.3 \pm 31.1	10-97	4	76.3 \pm 100.6	19-227	.247
	Prospective			Retrospective			
Total subjects	17	57.8 \pm 40.4	24-174	52	94.3 \pm 65.6	10-276	.003
Surgical subjects	17	45.0 \pm 32.7	10-132	52	84.7 \pm 63.5	5-276	.001
Control subjects	7	31.0 \pm 26.2	10-87	7	71.6 \pm 73.8	10-227	.085
BLA sample size	13	45.8 \pm 35.1	10-132	34	83.8 \pm 65.2	5-276	.005
LA sample size	5	33.8 \pm 20.5	21-70	19	76.2 \pm 62.0	13-234	.006

SD, Standard deviation; *BLA*, bilateral; *LA*, left atrial.

Patient Survival and Freedom From AF by Temporal Score

When stratified by temporal score, both prospective and retrospective studies demonstrated similar survival rates at 1, 2, and 3 years (Table 5), with prospective studies slightly better (range of 95.2%-96.1% vs range of 94.3%-91.9%). Retrospective studies, however, demonstrated increased rates of freedom from AF (range of 91.4%-87.3% vs range of 86.3%-79.4%).

Discussion

The use of meta-analyses to summarize research is not a novel approach but is still a vastly underused research tool. Ideally, investigators would pool individual data from multiple studies under various hypotheses either similar or identical to those of their original respective study. Usually, however, results from published reports are abstracted through the use of statistics on the basis of sampling methods.^{70,71} Results are pooled, and effect sizes can then be generated as if all studies were generated from one large hypothetical patient population, with each study acting as a

unique sample from that hypothetical population. The literature addressing the surgical treatment for AF now has dozens of studies on various populations from various highly regarded surgical groups, all producing excellent results. In this report we present the results of what we believe to be the first large-scale meta-analysis designed to evaluate the efficacy of surgical ablation as a treatment for the elimination of AF.

Our results suggest that both surgical groups with and without ablation experience nearly identical postoperative survival rates and superior freedom from AF rates at 3 months and 1, 2, and 3 years. Furthermore, among surgical patients, biatrial ablation procedures were similar to left atrial ablation—only procedures in postoperative survival and superior in freedom from AF rates. The higher success rate in ablating AF by applying the maze procedure or any other biatrial surgical modification is not surprising. Review of the current literature that discusses the electrophysiology of AF reveals that there are quite a few different mechanism suggested, from simple mechanisms pointing to the pulmo-

TABLE 3. Average weighted reported postoperative survival and freedom from recurrent atrial fibrillation, all patients

	Surgical subjects			Control subjects			<i>P</i> value
	No. of studies	Total sample size	Mean \pm SD*	No. of studies	Total sample size	Mean \pm SD*	
1-y survival	52	3841	94.5 \pm 0.0	11	429	97.8 \pm 0.0	.001
2-y survival	18	1313	94.1 \pm 0.0	5	299	97.7 \pm 0.0	.001
3-y survival	17	1338	92.5 \pm 0.0	6	334	95.1 \pm 0.0	.001
3-mo freedom from AF	39	2742	90.4 \pm 6.0	7	236	47.2 \pm 17.2	.001
1-y freedom from AF	37	3225	84.5 \pm 10.3	10	312	30.8 \pm 19.6	.001
2-y freedom from AF	21	1739	84.3 \pm 5.9	5	181	39.7 \pm 21.6	.001
3-y freedom from AF	18	1801	85.4 \pm 5.3	6	514	60.9 \pm 31.0	.013

SD, Standard deviation; *AF*, atrial fibrillation. *Sample weighted mean and corrected standard deviation.

TABLE 4. Average weighted reported postoperative survival and freedom from recurrent atrial fibrillation by lesion

	Biatrial			Left Atrial			P value
	No. of studies	Total sample size	Mean \pm SD*	No. of studies	Total sample size	Mean \pm SD*	
Surgical subjects							
1-y survival	32	2391	94.9 \pm 0.0	20	1450	93.9 \pm 0.0	.999
2-y survival	14	1159	94.2 \pm 0.0	4	154	92.8 \pm 0.0	.999
3-y survival	13	1136	92.8 \pm 0.0	3	148	89.4 \pm 0.0	.500
3-mo freedom from AF	23	1985	92.0 \pm 4.0	16	757	86.1 \pm 8.4	.001
1-y freedom from AF	24	2260	88.9 \pm 8.2	13	965	75.9 \pm 8.4	.001
2-y freedom from AF	15	1523	85.8 \pm 5.0	6	216	74.5 \pm 1.9	.001
3-y freedom from AF	16	1684	87.1 \pm 4.7	2	117	73.4 \pm 0.0	.001
Control subjects							
1-y survival	9	378	97.9 \pm 0.0	2	51	97.4 \pm 0.0	.999
2-y survival	5	299	97.7 \pm 0.0	—	—	—	—
3-y survival	6	334	95.1 \pm 0.0	—	—	—	—
3-mo freedom from AF	5	185	48.3 \pm 14.9	2	51	43.2 \pm 24.2	.076
1-y freedom from AF	7	234	32.8 \pm 18.4	3	78	26.8 \pm 21.5	.014
2-y freedom from AF	4	149	35.4 \pm 20.5	1	32	66.2 \pm 0.0	.001
3-y freedom from AF	5	287	53.1 \pm 34.5	1	227	78.8 \pm 0.0	.001

SD, Standard deviation; AF, atrial fibrillation. *Sample weighted mean and corrected standard deviation.

nary veins as the source of the arrhythmia to a more complex pattern showing that pathophysiology is more complex and biatrial.^{72,73}

A better understanding for the possible reason for the differences in the mechanisms is important. Unfortunately, to some extent, our ability to do so is presently limited. In

this study the results with the biatrial approach were superior to those achieved with left atrial ablation only. This might be related to the fact that the surgical patients usually presented with other cardiac pathologies, such as mitral valve and coronary artery disease, and with long duration of AF. As a result, the disease process in the surgical group of

TABLE 5. Average weighted reported postoperative survival and freedom from recurrent atrial fibrillation by temporal score

	Prospective			Retrospective			P value
	No. of studies	Total sample size	Mean \pm SD*	No. of studies	Total sample size	Mean \pm SD*	
Surgical subjects							
1-y survival	13	560	95.2 \pm 0.0	39	3281	94.3 \pm 0.0	.900
2-y survival	4	234	99.4 \pm 0.0	14	1079	92.8 \pm 0.0	.003
3-y survival	2	157	96.1 \pm 0.0	14	1127	91.9 \pm 0.0	.956
3-mo freedom from AF	10	459	86.3 \pm 4.4	29	2283	91.4 \pm 5.8	.003
1-y freedom from AF	10	459	85.1 \pm 3.7	27	2735	84.8 \pm 9.7	.375
2-y freedom from AF	10	459	70.1 \pm 5.7	14	1395	85.2 \pm 5.3	.072
3-y freedom from AF	2	168	79.4 \pm 0.0	16	1633	87.3 \pm 5.3	.095
Control subjects							
1-y survival	7	217	96.5 \pm 0.0	4	212	97.1 \pm 0.0	.990
2-y survival	1	87	100.0 \pm 0.0	4	212	96.6 \pm 0.0	.995
3-y survival	1	87	100.0 \pm 0.0	5	247	93.1 \pm 0.0	.995
3-mo freedom from AF	5	168	44.4 \pm 16.9	2	68	54.9 \pm 15.6	.001
1-y freedom from AF	7	217	31.4 \pm 16.9	3	95	30.0 \pm 23.5	.300
2-y freedom from AF	2	66	31.1 \pm 28.5	3	115	44.2 \pm 15.2	.242
3-y freedom from AF	1	87	25.6 \pm 0.0	5	427	71.3 \pm 27.7	.003

SD, Standard deviation; AF, atrial fibrillation. *Sample weighted mean and corrected standard deviation.

patients is much more advanced and diffuse when compared with that of patients treated with catheter pulmonary vein ablation for lone AF. Given that most mapping data for AF are based on nonsurgical patients with lone AF, it would be difficult to speculate about the exact mechanism among surgical patients to further support either surgical approach. Mapping during surgical intervention has the potential to guide surgeons to more specific ablation protocols. However, at this time, few clinical studies have assessed this strategy.

There are some reports documenting greater permanent pacemaker implantation after the maze procedure compared with that after left atrial ablation only. The indication for pacemaker use is sinus node dysfunction in most cases. The majority of patients with sinus node activity recover to the extent that patients are no longer pacemaker dependent.⁷⁴ However, except for among patients after the maze I procedure, sinus node dysfunction cannot be attributed to the surgical procedure. It might be due to the fact that there is a higher success rate in ablating AF and that more cases of sick sinus syndrome that are strongly associated with AF are discovered.

Our study has several strengths and limitations. To our knowledge, this is the first attempt to systematically analyze published data for the surgical treatment of AF. We have conducted an extensive search for all clinical studies meeting our search criteria. However, publication bias might have eliminated potential studies for whatever reason deemed important by various editorial boards, and although there is no formal way to test for this, we would be remiss if we did not caution the readers of this potential for bias. In addition, determining rates of survival and freedom from postoperative AF was sometimes accomplished by viewing actual Kaplan-Meier curves and extrapolating results. This might have led to some discrepancies from the true published results. However, given the ease of reading a Kaplan-Meier plot, we think this is a minimal concern. Furthermore, our study included all studies relevant to our search strategy.

We made no attempt to exclude studies on the basis of size, degree of follow-up, or definition of AF. This might have biased our findings, but we have attempted to portray as general and inclusive a review of the literature as possible. The inclusion of different study groups might have biased the effects of any subgroup analysis, but we believe this effect could be minimal because of the consistent profile of patients referred for a surgical ablation procedure. Studies involving shorter follow-up might have ended before a return to dysrhythmia, thereby indicating artificially high rates of freedom from AF. Unfortunately, the traditional strengths of meta-analyses involving clinical trials are potential limitations for our study. Those meta-analyses have very defined patient groups from which a meta-analysis can be performed. There are few clinical trials involv-

ing our subject matter, leaving us with retrospective trials from which patient groups were undoubtedly more heterogeneous. With this in mind, we have attempted to give the interested reader a composite view of the existing research regarding surgical treatment for AF.

We caution the reader that this is a summary of published results. We did not have access to original data, and thus errors might have occurred in our extrapolation of data from Kaplan-Meier tables, in the combination of multiple control groups into one group through weighting, and in the potential temporal bias of using data over an 11-year span. Surgical ablation expertise and technique have no doubt caused increases in both survival and freedom from AF rates. Furthermore, freedom from AF as a study end point was generally defined as a return to sinus rhythm, with no additional detail. It is possible that a different patient population would have provided different freedom from AF rates under different investigator protocols.

This summary review suggests the surgical treatment for AF offers similar postoperative survival rates and vastly superior freedom from AF rates compared with those of traditional therapies. In addition, the surgical treatment of AF involving biatrial status offers superior long-term survival and freedom from AF.

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